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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/690,713	10/22/2003	Timothy C. Thompson	PRO025/4-9CON2US	9759
21586 7590 05/17/2007 VINSON & ELKINS, L.L.P. 1001 FANNIN STREET 2300 FIRST CITY TOWER HOUSTON, TX 77002-6760			EXAMINER YAO, LEI	
			ART UNIT 1642	PAPER NUMBER
			MAIL DATE 05/17/2007	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/690,713	<b>Applicant(s)</b> THOMPSON, TIMOTHY C.	
	<b>Examiner</b> Lei Yao, Ph.D.	<b>Art Unit</b> 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☐ Responsive to communication(s) filed on 3/7/2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 26-39 is/are pending in the application.  
     4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 26-39 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
     a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>10/22/2003</u> | 6) <input type="checkbox"/> Other: _____  |

Art Unit: 1642

## **DETAILED ACTION**

### ***Election/Restrictions***

Applicant's election without traverse of group I (claims 26-39), a method treating a subject having a neoplastic disorder comprising administering an anti-caveolin antibody, in the reply filed on 3/7/2007 is acknowledged.

Claims 1-25 and 40-105 are cancelled. Claims 26-39 are pending and examined on the merits.

### ***Priority***

This application claims benefit of application No. 10151055 filed on 5/21/2002, 09797969 filed on 3/5/2001, 09186184 filed on 11/05/1998, and 60064351 filed on 11/05/1997, which are acknowledged.

### ***Information Disclosure Statement***

The information disclosure statement (s) (IDS) submitted on 10/22/2003 are/is considered by the examiner and initialed copies/copy of the PTO-1449 are/is enclosed.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the **first paragraph of 35 U.S.C. 112**:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 26-39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether undue experimentation is required, are summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed

Art Unit: 1642

in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The claims are drawn to a method for treating a subject having neoplastic disorder or disease of prostate comprising administering to the subject a composition comprising an anti-caveolin antibody wherein the antibody effective to inhibit metastasis in the neoplastic disorder. To satisfy the requirement of 112, 1st paragraph, it is necessary that the specification provide an enabling disclosure of how to make and use a claimed invention. Thus, it would be expected that one of skill in the art would be able to treat a neoplastic disorder comprising prostate or breast cancer with any antibody to caveolin without undue experimentation by using the claimed method.

The specification teaches caveolin and expression of caveolin in human prostate cancers by immunoassay and correlation of caveolin expression and androgen sensitivity (page 34-36). However, the specification does not provide a method of treating prostate cancer or any neoplastic disorder by administering to the subject an anti-caveolin antibody. There are no working examples to guide or assist the skilled artisan in practicing the claimed method of treating such neoplastic disorder comprising prostate disease with an antibody to caveolin.

The instant specification provides insufficient guidance or direction to predictably enable one of ordinary skill in the art to use the invention as claimed. Those of skill in the art recognize the unpredictability of treating tumors with antibodies. For example, Jain R. K. (Scientific American, 271(1): 58-65, July 1994) discloses the art known barriers to the delivery of drugs into solid tumors. These impediments include (1) Non-uniform blood delivery to all areas of the tumor in which some areas of the tumor receive therapeutic agents and other areas of the tumor receive no therapeutic agent at all. (Page 60 col. 3); (2) Increased viscosity of blood in the tumor itself which also hinders drug delivery to the tumor (see paragraph bridging pages 60 and 61); (3) High liquid pressures in the interstitial matrix can retard the delivery of large therapeutic agents, such as antibodies, into tumors (page 61, Col. 1 paragraph 1); (4) Convection is a necessary mechanism by which larger therapeutic molecules such as antibodies, reach target cells which are not directly fed by the vasculature. Convection is not observed in large tumors

Art Unit: 1642

(defined as more than ½ centimeter in diameter, page 62 col. 1) and convection is necessary for adequate drug delivery of molecules having a molecular weight of more than 5000 (page 61, col. 1 through page 63, col. 3) and (4) Molecules as large as antibodies (i.e., MW=150,000) would require several months to reach a uniform concentration in a tumor that measures 1 centimeter in radius (page 63, col. 2). Further, Dillman R. O., (Annals of Internal Medicine, 111:592-603, 1989) summarizes (see abstract) the status of in-vivo use of monoclonal antibodies for treating cancer wherein despite advances in biotechnology, many major hurdles persist including tumor cell heterogeneity, lack of cytotoxicity, and the development of human anti-mouse antibodies (HAMA). Also, Weiner L. M. (Seminars in Oncology, 26 (4 Suppl 12): 41-50, August 1999) provided an overview of monoclonal antibody therapy including some promising activity, however, major obstacles to clinical efficacy still exist extending the unpredictability of this treatment. This includes impaired distribution and delivery of antibody to the tumor site, inadequate trafficking of potential cellular effectors to tumor, antigenic heterogeneity, shed or internalized targets and insufficient target specificity (see page 43). Furthermore, as disclosed by Dillman, R. O. (Journal of Clinical Oncology, 12(7):1497-1515, 1994) discloses, after reviewing the literature on the use of unconjugated monoclonal antibodies to treat cancer, that "at present, there are no unconjugated monoclonal antibodies that have proven therapeutic benefit in hematologic malignancies or solid tumors." Thus, absent objective evidence to the contrary, it is highly unpredictable that applicant's unconjugated antibody would possess any therapeutic effects.

Moreover, the prior art does not provide convinced evidence that caveolin is directly related with tumorigenesis and is useful therapeutic target. For example, Nelson, J., teaches that progression of caveolin-depleted tumors is less than control tumors, but the tumor still progress, and that such therapy might be considered ineffective (Nelson, J. B. Nature Medicine, 4:1011-1012, 1998, page 1011, 3<sup>rd</sup> col). Additionally, the prior art has not settled the question of the biological function of caveolin in neoplastic disorder comprising prostate or breast cancer. For example, Lee et al., (Oncogene, vol 16, page 1391-1397, 1998) teach that caveolin expression is significantly reduced in human breast cancer cell compared with their normal mammary epithelial counter-parts (abstract, line 9-12).

Art Unit: 1642

No direction or guidance is provided in current specification to assist one skilled in the art using an antibody to caveolin in a method of treating neoplastic disorder comprising prostate or breast disease in a subject. In view of the lack of the predictability of the art to which the invention pertains as evidenced by the art of Jain R. K., Dillman R. O., Weiner, Dillman, Nelson, Lee et al., and the lack of established clinical protocols for effective immunotherapy, one skilled in the art would be forced into under experimentation in order to practice the claimed invention.

### **Conclusion**

No claims are allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Yang et al., (Clinical Cancer Research, vol 4, page 1873-1880, August, 1998)) disclose that elevated expression of caveolin is associated with prostate and breast cancer (entire paper). Yang et al., do not teach or suggest a method of treating any neoplastic disorder by administering to the subject a composition comprising an anti-caveolin antibody.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lei Yao, Ph.D. whose telephone number is 571-272-3112. The examiner can normally be reached on 8am-6.00pm Monday-Thursday.


Any inquiry of a general nature, matching or file papers or relating to the status of this application or proceeding should be directed to Kim Downing for Art Unit 1642 whose telephone number is 571-272-0521

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lei Yao,  
Examiner  
Art Unit 1642

LY

  
SHANON FOLEY  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600